REMARKS

Claims 3, 7-13 and 16-18 are pending and under examination. Applicants have not added, canceled or amended any claims. Accordingly, upon consideration of this Communication, claims 3, 7-13 and 16-18 will still be pending and under examination.

The October 5, 2005 Interview

Applicants wish to thank the Examiner for his time and consideration during the October 5, 2005 telephonic interview. The contents of that interview are discussed below.

The Claimed Invention

The subject invention provides a method for treating inflammation in a subject which comprises administering to the subject an agent selected from the group consisting of soluble receptor for advanced glycation endproduct (sRAGE) or anti-RAGE antibody or anti-EN-RAGE $F(ab')_2$ fragment in an amount which inhibits the interaction between receptor for advanced glycation endproduct (RAGE) and EN-RAGE, thereby treating inflammation in the subject.

Rejection under 35 U.S.C. §103(a)

In the April 12, 2005 Final Office Action, and as maintained in the August 29, 2005 Advisory Action, the Examiner rejected claims 3-5 and 11-14 under 35 U.S.C. §103(a), as allegedly obvious over United States Patent No. 5,864,018 ("Morser") in view of Ritthaler et al. (Amer. J. Path., 146(3):668-694, 1995) ("Ritthaler").

In response to this rejection, applicants respectfully traverse.

Applicants again maintain that even if RAGE/AGE binding were "implicated in inflammation," there would have been no reasonable expectation of success that an agent which inhibits EN-RAGE binding to RAGE would inhibit inflammation absent experimentation.

During the October 5, 2005 telephonic interview, and regarding this position, the Examiner indicated that he would consider persuasive any evidence indicating that there would have been no reasonable expectation that treating inflammation by inhibiting RAGE/AGE binding would succeed, despite alleged teachings that RAGE/AGE binding is "implicated in inflammation."

Accordingly, applicants submit as **Exhibit A** Liotta, et al. ("Cancer: Checkpoint for Invasion", Nature 405:287-288 (2000)) ("Liotta").

In relevant part, Liotta discusses the discovery that RAGE and amphoterin are a receptor-ligand pair that plays a role in tumor cell invasiveness, growth and movement (see first paragraph of Liotta). However, Liotta also indicates that the discovery of the RAGE/amphoterin pathway and its purported involvement in tumor metastasis does not mean that therapeutic methods targeting that pathway would necessarily be expected to succeed in treating the disorder. Specifically, Liotta states that "'[s]ignal-transduction therapy' is a treatment strategy in which key, hyperactive cellular signalling pathways that cause disease are targeted. The trick is to find a rheostat in the cell's circuitry that is not bypassed by collateral or compensatory paths" (last paragraph of Liotta).

Implicit in that text is the notion that for a given receptor-ligand pair whose binding is "implicated" in a disorder, it is uncertain, absent experimentation, whether inhibiting such binding can treat the disorder. This uncertainty derives, at least in part, from the possible existence of pathways which are collateral or compensatory to the pathway involving the receptor-ligand pair.

In view of this teaching, applicants maintain that absent the experiments performed in the subject application, there would have been no reasonable expectation that sRAGE, an anti-RAGE antibody or an anti-EN-RAGE antibody would inhibit inflammation. That is, until the experiments described in the subject application were performed, there would have been no reasonable expectation that the effect of inhibiting RAGE/AGE binding would not be bypassed by a collateral or compensatory pathway. The Examiner's assertion of obviousness based on the mere *implication* of RAGE/AGE interaction in inflammation does take into account this lack of predictability.

Accordingly, applicants maintain that the subject claims are not obvious over Morser in view Ritthaler, and therefore satisfy the requirements of 35 U.S.C. §103(a).

Further, the Examiner rejected claims 12, 13 and 16-18 under 35 U.S.C. §103(a) as allegedly obvious over Morser and Ritthaler in view of United States Patent No. 5,998,408 ("Baker").

Specifically, the Examiner asserts that it would have been obvious at the time of the invention to treat inflammation associated with autoimmune disease in a subject by inhibiting the interaction of AGE and RAGE by administering sRAGE or the anti-RAGE antibodies

disclosed by Morser. This allegedly is because Morser demonstrates that sRAGE or anti-RAGE antibodies block the interaction between RAGE and its ligands, Ritthaler teaches that RAGE and its ligands are involved in the diseases involving inflammation and Baker teaches diseases involving inflammation, specifically the autoimmune process.

In response to the Examiner's rejection, applicants respectfully traverse.

Claims 12, 13 and 16-18 are dependant on claim 3 which is discussed above. Thus, these claims possess all limitations of claim 3.

The non-obviousness of claim 3 over Morser and Ritthaler is discussed above. Baker, which according to the Examiner merely teaches diseases involving inflammation, does not cure the deficiency of the other two references, in that it does not create a reasonable expectation of success. In sum, the reasons for nonobviousness of claim 3 apply to claims 12, 13 and 16-18.

Accordingly, applicants maintain that the subject claims are not obvious over Morser and Ritthaler in view of Baker, and therefore satisfy the requirements of 35 U.S.C. §103(a).

Obviousness-Type Double Patenting Rejection

The Examiner provisionally rejected claims 3-11 and 16 as allegedly unpatentable under the judicially created doctrine of obviousness-type double patenting over claims 47, 50, 55-60, 62-65 and 67 of copending U.S. Application No. 09/167,705 in view of United States

Patent No. 5,864,018 and Ritthaler et al. (1995). Applicants understand this rejection to apply to claims 3, 7-11 and 16. According to the Examiner, a timely filed terminal disclaimer in compliance with 37 C.F.R. §1.321(c) may be used to overcome a provisional rejection based on a nonstatutory double patenting ground.

In response, but without conceding the correctness of the Examiner's rejection, applicants will consider submitting a terminal disclaimer for claims 3, 7-11 and 16 once the rejection is no longer provisional.

Summary

For the reasons set forth hereinabove, applicants respectfully request that all the claims of this application be allowed, and that the application proceed to issuance.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee, other than the enclosed sum of $455.00, is deemed necessary in connection with the filing of this Communication. However, if any additional fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

John P. White
Registration No. 28,678
Alan J. Morrison
Registration No. 37,399
Attorneys for Applicants
Cooper & Dunham LLP
1185 Avenue of the Americas
New York, New York 10036
Tel. No. (212) 278-0400

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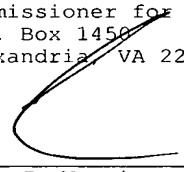

12/13/05

Alan J. Morrison Date
Reg. No. 37,399